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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,376	03/09/2001	Gary Van Nest	377882001700	8397

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,376	NEST ET AL.	
	Examin r	Art Unit	
	Jane Zara	1635	

-- Th MAILING DATE of this communication appears on the cov r she t with the corr spondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *12-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 56-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office action is in response to the communication filed 8-7-03.

Claims 1-66 are pending in the instant application.

Election/Restrictions

This application contains claims 12-55, drawn to an invention nonelected with traverse 2-20-03. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Arguments

Withdrawn Rejections

Applicant's arguments, see Remarks, filed 8-7-03, with respect to claims 1-11 and 56-66 have been fully considered and are persuasive. The written description and 112, second paragraph rejections of claims 1-11 and 56-66 has been withdrawn.

Applicant's arguments with respect to the prior art rejections of claims 1-11, 56-66 have been considered but are moot in view of the new ground(s) of rejection.

Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Uhlen.

Uhlen teaches an immunomodulatory polynucleotide/microcarrier complex, comprising an ISS comprising the sequence 5'-C,G-3' covalently linked to the surface of a nonbiodegradable, solid phase microcarrier 25nm and 5 um in size (See col. 5, line 20-col. 9, line 12; SEQ ID Nos. 2, 4, 14).

Claim Rejections - 35 USC § 103

Claims 1-11 and 56-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al, in view of the combined teachings of Schreiner et al, Nantz et al, and Uhlen.

The claims are drawn to compositions or kits comprising an immunomodulatory polynucleotide/microcarrier complex comprising a polynucleotide linked either non-covalently or covalently to either a liquid or solid phase carrier, between 25nm and 5um in size, and which immunomodulatory polynucleotide 5' -C-G-3', and 5'-T-C-G-3', 5'-purine,purine,C,G,pyrimidine,pyrimidine-3', or 5'-T,C,G-3 or SEQ ID NO: 1.

Schwartz et al teach immunomodulatory polynucleotide/microcarrier complexes comprising an antigen, immunostimulatory sequences 5' -C-G-3', and 5'-T-C-G-3', 5'-purine,purine,C,G,pyrimidine,pyrimidine-3', or 5'-T,C,G-3 or SEQ ID NO: 1, which complexes are or between 5um and 25nm in size (See pages 4-6, 12, 15-16, and table I on page 29; see accompanying sequence alignment data).

Schwartz et al do not teach non-encapsulated polynucleotide/microcarrier complexes, nor covalently linked polynucleotide/microcarrier complexes, nor solid phase microcarriers.

Schreiner et al teach polynucleotide/microcarrier complexes, which polynucleotide is linked to the surface of a nonbiodegradable microcarrier, and which microcarrier is a lipid phase microcarrier, and which complexes comprise either non-covalent or covalent linkages (See col. 17, line 57-col. 18, line 53

Nantz et al teach polynucleotide microcarrier complexes for cellular delivery comprising liquid and solid phase microcarriers covalently or non-covalently linked to the polynucleotide (see entire document, esp. col. 3-6; col. 17, line 38-col. 23, line 20).

Uhlen teaches immunomodulatory polynucleotide/microcarrier complexes, comprising an immunomodulatory polynucleotide comprising the sequence 5'-C,G-3' covalently linked to the surface of a nonbiodegradable, solid phase microcarrier 25nm and 5 um in size (See col. 5, line 20-col. 9, line 12; SEQ ID Nos. 2, 4, 14).

It would have been obvious to one of ordinary skill in the art to prepare immunomodulatory polynucleotide/microcarrier compositions comprising the immunostimulatory sequences 5' -C-G-3', and 5'-T-C-G-3', 5'-purine,purine,C,G,pyrimidine,pyrimidine-3', or 5'-T,C,G-3 or SEQ ID NO: 1 and a solid or liquid phase microcarrier because the immunomodulatory polynucleotides comprising 5' -C-G-3', and 5'-T-C-G-3', 5'- purine,purine,C,G,pyrimidine,pyrimidine-3', or 5'-T,C,G-3 or SEQ ID NO: 1 have been taught by Schwartz et al and polynucleotide/microcarrier complexes have been routinely used in the art for target cell delivery of polynucleotides and have been taught previously by Schreiner et al, Nantz et al, and Uhlen. One of ordinary skill in the art would have been motivated to prepare and use immunomodulatory polynucleotide/microcarrier compositions for target cell delivery of

polynucleotides because immunomodulatory effects of the immunomodulatory polynucleotides are exhibited after target cell delivery and uptake, and the microcarriers enhance target cell uptake and intracellular delivery of polynucleotides, as has been taught previously by many in the prior art including Schreiner et al and Nantz et al. One of ordinary skill in the art would have been motivated to utilize the polynucleotides comprising 5' -C-G-3', and 5'-T-C-G-3', 5'- purine,purine,C,G,pyrimidine,pyrimidine-3', or 5'-T,C,G-3 or SEQ ID NO: 1 for target cell delivery because Schwartz et al teach that polynucleotides comprising this motif have led to immunomodulatory effects of target cells, and have lead to a desired immune response by target cells. One of ordinary skill in the art would have expected the enhanced target cell delivery and uptake of the polynucleotide/microcarrier complexes compared to naked polynucleotides because it was taught by Schreiner et al and Nantz et al, and it is well known in the art that enhanced polynucleotide delivery occurs with nucleic acid/microcarrier complexes because the complexes better penetrate the target cell's membrane, providing increased intracellular delivery compared to naked polynucleotides introduced to target cells. And one of ordinary skill in the art would also have expected that efficient intracellular delivery of polynucleotides comprising the immunomodulatory motif comprising 5' -C-G-3', and 5'-T-C-G-3', 5'- purine,purine,C,G,pyrimidine,pyrimidine-3', or 5'-T,C,G-3 or SEQ ID NO: 1 would enhance the immunomodulation of the target cell following intracellular delivery of the polynucleotide/microcarrier complexes. One of ordinary skill in the art would have been motivated to covalently link polynucleotides to the microcarrier for delivery to particular target cells in some instances because

covalent linkages enhance the stability of the complex in desired target cells and these target cells then degrade linkages between the microcarrier and the polynucleotide, allowing for intracellular release and activity of the immunomodulatory polynucleotides under appropriate biological conditions. One of ordinary skill in the art would have been motivated to optionally prepare non-covalently or covalently linked complexes for delivery to a particular type of target cell because the stability of the non-covalently linked complexes are stable enough to remain intact for sufficient target cell delivery in appropriate biological conditions, non-covalent and covalent complexes have both been taught by Nantz and Schreiner and, depending on the choice of the appropriate target cell, either linkage would be a design choice for a particular polynucleotide/microcarrier complex for that particular target cell or biological situation.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

November 14, 2003

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER